PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61M 15/00 — A1

(11) International Publication Number: WO 95/20414

(43) International Publication Date: 3 August 1995 (03.08.95)

(21) International Application Number: PCT/SE95/00058

(22) International Filing Date: 23 January 1995 (23.01.95)

(30) Priority Data:
9400257-3 27 January 1994 (27.01.94) SE

(71) Applicant *(for all designated States except US)*: ASTRA AKTIEBOLAG [SE/SE]; S-151 85 Södertälje (SE).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: BERG, Elna, Birgitta [SE/SE]; Dalby nr 10, S-240 10 Dalby (SE). NILSSON, Hans, Jörgen [SE/SE]; Hjalmar Gullbergs väg 24, S-224 66 Lund (SE).

(74) Common Representative: ASTRA AKTIEBOLAG; Patent Department, S-151 85 Södertälje (SE).

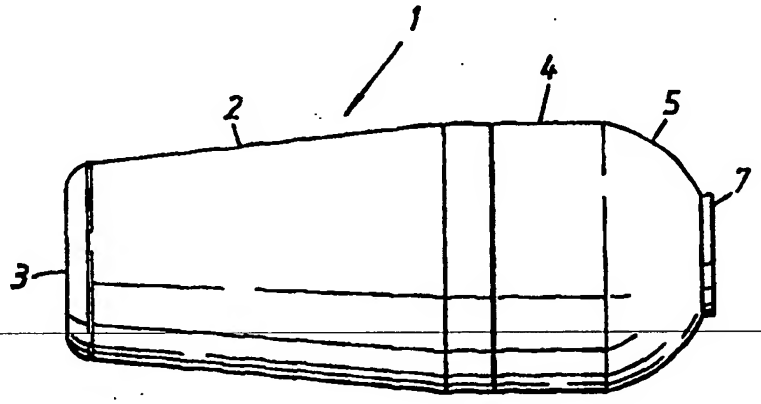
(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: AN INHALATION CHAMBER FOR CHILDREN FOR USE IN CONJUNCTION WITH A METERED DOSE INHALER

(57) Abstract

The present invention relates to a spacer for children primarily intended to be used in conjunction with a metered dose inhaler (MDI), said spacer having a generally oblong shape and being rotationally symmetrical around a central, longitudinal axis and being provided with an opening at each end located centrally in said axis for connection of a metered dose inhaler respectively of a mouth-piece or similar. The spacer has a small total volume which is in the range between 50 and 400 ml, and the material in the spacer has a surface resistivity which is lower than 10^9 Ohm, preferably lower than 10^6 Ohm.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	**GB**	United Kingdom	**MR**	Mauritania
AU	Australia	**GE**	Georgia	**MW**	Malawi
BB	Barbados	**GN**	Guinea	**NE**	Niger
BE	Belgium	**GR**	Greece	**NL**	Netherlands
BF	Burkina Faso	**HU**	Hungary	**NO**	Norway
BG	Bulgaria	**IE**	Ireland	**NZ**	New Zealand
BJ	Benin	**IT**	Italy	**PL**	Poland
BR	Brazil	**JP**	Japan	**PT**	Portugal
BY	Belarus	**KE**	Kenya	**RO**	Romania
CA	Canada	**KG**	Kyrgystan	**RU**	Russian Federation
CF	Central African Republic	**KP**	Democratic People's Republic of Korea	**SD**	Sudan
CG	Congo			**SE**	Sweden
CH	Switzerland	**KR**	Republic of Korea	**SI**	Slovenia
CI	Côte d'Ivoire	**KZ**	Kazakhstan	**SK**	Slovakia
CM	Cameroon	**LI**	Liechtenstein	**SN**	Senegal
CN	China	**LK**	Sri Lanka	**TD**	Chad
CS	Czechoslovakia	**LU**	Luxembourg	**TG**	Togo
CZ	Czech Republic	**LV**	Latvia	**TJ**	Tajikistan
DE	Germany	**MC**	Monaco	**TT**	Trinidad and Tobago
DK	Denmark	**MD**	Republic of Moldova	**UA**	Ukraine
ES	Spain	**MG**	Madagascar	**US**	United States of America
FI	Finland	**ML**	Mali	**UZ**	Uzbekistan
FR	France	**MN**	Mongolia	**VN**	Viet Nam
GA	Gabon				

AN INHALATION CHAMBER FOR CHILDREN FOR USE IN CONJUNCTION WITH A METERED DOSE INHALER

Technical field of the invention

The present invention relates to an oblong spacer for children primarily intended to be used in conjunction with a metered dose inhaler (MDI), said spacer being rotationally symmetrical around a central, longitudinal axis and being provided with an opening at each end located centrally in said axis for connection of an MDI respectively a mouth-piece or similar.

Background of the invention

MDI:s are containers with an actuating, metering valve containing a mixture of a pressurized propellant and a drug. When the valve is actuated, a dose of the drug/propellant mixture is ejected into the air and can be inhaled by a patient.

In order to alleviate the problems of a high oral deposition and the coordination difficulties associated with MDI:s, different kinds of spacer devices have been developed, that is a holding chamber connected to the MDI at one end. The other end of the spacer is connected to or provided with a mouthpiece and/or a face mask through which a patient can inhale. When the valve is actuated, the dose of the drug/propellant mixture is sprayed into the spacer, resulting in that a cloud of smaller particles in the respirable range (an aerosol) is contained in the chamber for a certain time, during which time larger particles, that is

particles that normally would be deposited orally, are separated from the aerosol dose and deposited in the spacer. The propellant evaporates at the same time. The cloud of particles can be inhaled effortlessly by the patient.

The prior art devices of this kind are however exclusively designed for use in older children and adults. Their volume normally varies from 0.5 to 2 litres and they mostly are made of a polymer material, for instance polycarbonate. They are often adapted for use in younger children. The reproducibility and age-dependency of their dose-delivery when used for the treatment of children is important, but are not yet ascertained. Theoretical models have predicted an increased lung deposition in small children due to the smaller airway calibre and a greater ventilation/kg, but in vivo documentation is sparse. Most of the available documentation in vivo of dose delivery from the prior art devices discusses the clinical response in wheezy children from inhalations of β_2-agonist. In these, the drug has been administered in doses considerably above the minimum effective dose. The response is therefore not critically dependent on reproducible delivery. The results from studies relating to these drugs further can not be extrapolated to the generation of a steroid aerosol, which has other micronizing and solubility characteristics.

Consequently there is a need for spacer delivery systems specially adapted to the treatment of young children. The need is particularly great in systems to be used in the administering of steroids due to the

stricter demands on the reproducability and dosis accuracy for these drugs. A high utilisation of the substance also is desirable.

The volume of the spacer is critical since the aerosol is emptied from the chamber in an exponential manner. The inspiratory volume required to inhale the total dose of aerosol will be several times the spacer volume. The settling of particles limits the time available for inhalation. Since the inspirational capability of small children is smaller than the inspirational capability of adults, a reduction of the spacer volume might be indicated, for instance in the range of a few tidal breaths of an infant to reduce the time required for administration.

A reduced spacer volume will however contain an increased concentration of aerosols, and, accordingly, will require less time to empty. The fraction of airborne particles is however reduced due to impaction, adsorption, sedimentation and coagulation of the aerosol. This tendency will be aggravated if the spacer is made of a polymer material like polycarbonate, which may be charged by electrostatic forces, since the distance for each particle to the nearest wall will be smaller than in a prior art spacer, and the electrostatic forces will consequently have a greater influence.

The object of the invention consequently is to provide a spacer well adapted to the treatment of small children based on the above considerations.

Short description of the inventive concept

The above object is achieved in that a spacer as described introductorily is designed to have a small total volume which is in the range between 50 and 400 ml, and in that the material in the spacer has a surface resitivity which is lower than 10^9 Ohm, preferably lower than 10^6 Ohm. In a most preferred embodiment the surface resistivity is lower than 1. Other preferred embodiments are set forth in the dependent claims.

Brief description of the appended drawings

Fig 1 shows a spacer according to the invention in a side view,
Fig 2 illustrates the narrow end of the spacer to which an MDI is to be connected
Fig 3 shows the broad end of the spacer.

Detailed description of a preferred embodiment of the invention

Fig 1 shows the preferred spacer 1 which has an oblong shape with a slightly conically tapering first part 2 with a first end surface 3, a central, cylindrical part 4 and a substantially hemispherical second part 5. The junction between the surface 3 and the tapering part 2 is rounded. The spacer is circular in section and consequently is rotationally symmetrical. The overall length of the spacer is about 130 mm and the length of the tapering part is about 80 mm. The diameter of the end surface 3 is about 40 mm (the round part of the

junction with the part 2 being disregarded), the diameter of the cylindrical part 4 being about 55 mm. The volume of the spacer is 220 ml. These dimensions are adapted to fit most small children although other dimensions are conceivable. The length of the spacer is adapted to standard MDI:s in that the spacer is long enough to prevent that particles within the respirable range are sprayed onto the opposite walls of the device when the valve of the MDI is actuated.

The hemispherical part 5 is provided with a central opening 6 having a projecting, circumferential flange 7 for the attachment of a standard mouth-piece or a face mask. A two way valve may be connected between spacer and mouth-piece/mask. .

The end surface 3 is also provided with a central opening 8 having an elliptical shape adapted to a standard mouth-piece adapter of a standard aerosol dispenser or MDI.

The spacer is made of stainless steel, which is a material having a surface resistivity which is well below the maximum surface resistivity at which the spacer is sufficiently conductive to function properly and at which the risk for electrostatic attraction of the respirable particles to the walls of the spacer is minimized.

The use of stainless steel will also result in a very robust spacer which consequently also in this respect is very well adapted to the use in smaller children.

In use, the mouth piece adapter of the MDI is connected to the corresponding end of the spacer and the mouth-piece with the two-way valve is connected to the other end. The two-way valve is designed to allow the inspirational air to flow through the spacer from the MDI to the mouthpiece but to prevent the expirational air to flow from the mouth-piece, in this way creating a rectified inspiration through the spacer. The inspirational air is sucked through the mouth piece adapter of the MDI though the standard air openings provided therein for ordinary use without spacer.

The rectified air flow in conjunction with the low risk for electrostatic influence on the respirable particles and the small volume of air which has to be inhaled will contribute to the deposition of a reasonably reproducable and accurate dosage in the desired locations in the lungs of the child, as well as also contributing to the achievement of the utilisation of a larger part of the drug than possible in standard prior art devices.

Possible modifications of the invention

The invention of course can be modified in many ways within the scope of the appended claims.

The desired surface resistivity characteristics can be obtained in several ways.

Thus, it is possible to use most metals, any polymer materials having a surface resistivity below the desired values, polymers containing additives giving

the desired chacteristics and polymers having been given the desired characteristics by means of a surface treatment.

CLAIMS

1. Spacer for children primarily intended to be used in conjunction with a metered dose inhaler (MDI), said spacer having a generally oblong shape and being rotationally symmetrical around a central, longitudinal axis and being provided with an opening at each end located centrally in said axis for connection of an meterd dose inhaler respectively of a mouth-piece or similar, c h a r a c t e r i z e d in that said spacer has a small total volume which is in the range between 50 and 400 ml, and in that the material in the spacer has a surface resitivity which is lower than 10^9 Ohm, preferably lower than 10^6 Ohm.

2. Spacer according to claim 1, c h a r a c t e r i z e d in that the surface resistivity is lower than 1.

Fig. 1

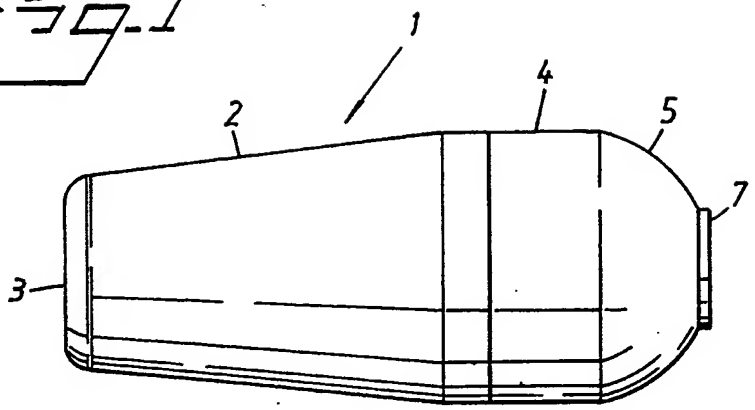


Fig. 2

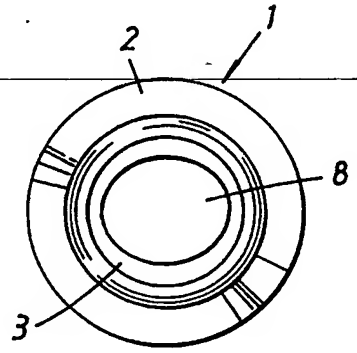
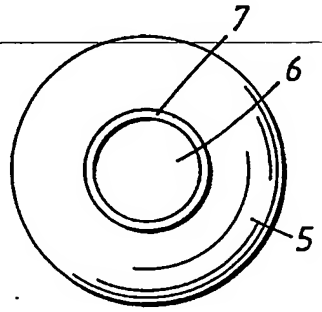


Fig. 3



INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 95/00058

A. CLASSIFICATION OF SUBJECT MATTER

IPC6: A61M 15/00
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SE, B, 411705 (AB DRACO), 4 February 1980 (04.02.80) --	1,2
A	WO, A1, 9316747 (BRAVO GALAN MANUEL), 2 Sept 1993 (02.09.93) --	1
A	GB, A, 2110543 (THE UNIVERSITY OF SOUTHAMPTON), 22 June 1983 (22.06.83) --	1
A	EP, A2, 0385212 (GAPLAST GMBH), 5 Sept 1990 (05.09.90) -- --------	1

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"B" erlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 April 1995	22 -05- 1995
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Anette Hall Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

Information on patent family members

25/02/95

International application No.
PCT/SE 95/00058

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
SE-B- 411705	04/02/80	AT-B- 369993	25/02/83
		AU-B- 514557	19/02/81
		AU-A- 3022677	10/05/79
		BE-A- 860626	09/05/78
		CA-A- 1077799	20/05/80
		CH-A- 623480	15/06/81
		DE-A,C- 2749629	11/05/78
		FR-A,B- 2369848	02/06/78
		GB-A- 1565029	16/04/80
		JP-C- 1328462	30/07/86
		JP-A- 53082089	20/07/78
		JP-B- 60051910	16/11/85
		LU-A- 78473	14/07/78
		NL-A- 7712354	11/05/78
		SE-A- 7612448	10/05/78
		US-A- 4174712	20/11/79
WO-A1- 9316747	02/09/93	NONE	
GB-A- 2110543	22/06/83	NONE	
EP-A2- 0385212	05/09/90	DE-U- 8902559	27/04/89